

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of claims:

1. (original) The DNA sequence 5'-CTCCTCCATGGTTATAAGGG-3' (SEQ ID NO: 9).
2. (original) The DNA sequence 5'-CCCAGAGTAAGAACATTATTC-3' (SEQ ID NO: 10).
3. (original) A variant paraoxonase protein having a substitution of isoleucine by valine, as coded by the codon 102 of exon 4 of the *PON1* gene.
4. (original) The variant protein according to claim 3 comprising the amino acid sequence of SEQ ID NO: 2.
5. (original) A capturing probe which comprises a single stranded polynucleotide comprising a nucleotide sequence encoding a variant human paraoxonase protein having a substitution of isoleucine by valine at the residue corresponding to position 102 of SEQ ID NO. 4.

6. (original) A capturing probe which comprises a single stranded polynucleotide comprising a nucleotide sequence encoding a human paraoxonase protein.

7. (original) A kit or assay comprising means for determining the presence or absence in a serum sample of a variant protein of claim 3.

8. (original) A transgenic non-human animal comprising a human DNA sequence comprising a nucleotide sequence encoding a variant paraoxonase protein having a Ile102Val substitution.

9. (Original) A method of phenotype-targeted gene sequencing and other mutation search methods, in which DNA samples of subjects are selected on the basis of phenotypic measurements of a protein concentration or enzyme activity of the protein encoded by the gene to be sequenced.

10. (new) A method for determining the presence in a biological sample of a DNA sequence comprising a nucleotide sequence encoding a variant paraoxonase protein, the method comprising determining the allelic pattern of the codon number 102 of a paraoxonase (PON1) encoding gene in the genomic DNA of the

sample, identification of an Ile102Val mutation indicating the presence of said DNA sequence.

11. (new) A method for screening a subject to determine if said subject is a carrier of at least one Ile102Val mutant paraoxonase gene comprising

- a) providing a biological sample of the subject to be screened,
- b) performing an assay for detecting in the biological sample the presence of the Ile102Val genotype of the human paraoxonase (*PON1*) gene,
- c) identifying as a carrier a subject providing a sample having at least one Ile102Val allele in the genotype.

12. (new) A method for assessing an individual's risk to develop cancer, coronary or cerebrovascular disease, hypertension, type 2 diabetes, dementia, arthrosis, cataract and sensitivity to organophosphorus compounds and/or altered effectiveness of a paraoxonase agonist or paraoxonase inducing or enhancing therapies in an individual, comprising

- a) providing a biological sample of the subject to be screened,

b) performing an assay for detecting in the biological sample the presence of the Ile102Val genotype of the human paraoxonase (*PON1*) gene,

c) identifying as an individual having increased risk of said disease, sensitivity to an organophosphorus compound or reduced effectiveness of a paraoxonase agonist or paraoxonase inducing or enhancing therapy, a subject providing a sample having at least one Ile102Val allele in the genotype.

13. (new) The method according to claim 9 or 10 wherein the allelic pattern is determined by an assay that analyzes a sample of DNA.

14. (new) The method according to claim 12 wherein the DNA sample is analyzed by hybridizing said DNA, or an amplification product thereof, to an immobilized nucleic acid in a multiplex format.

15. (new) A kit for performing the method according to claim 9 or 10, comprising means for determining the allelic pattern of codon 102 of a paraoxonase encoding (*PON1*) gene in a genomic DNA sample.